REMARKS

The amendment to the priority information is made to relinquish the priority claim of the present application to USSN 09/718,308. Applicants request that the term of any patent issued from this application be calculated beginning with International Patent Application PCT/US01/13471, filed April 26, 2001, as the first non-provisional priority document.

The amendment to the claims is voluntary and made at the option of the assignee as being of commercial interest for immediate patent protection. Applicants intend to pursue coverage for additional subject matter embodied in the disclosure and claims as originally filed in one or more separate applications.

Entry of the claim amendments does not introduce new matter into the disclosure. Support for the new claims may be found at various places in the specification, such as the following:

Claim 13:	Previous claims 1 & 6; page 4 lines 7-16; and throughout the disclosure
Claim 14:	Previous claim 2
Claim 15:	Previous claim 3
Claim 16:	Previous claim 7
Claim 17:	Page 17 lines 31-39; Table 7 (page 40)
Claim 18:	Page 18 lines 1-6; Table 7 (page 40)
Claim 19:	Page 15 line 37 to page 16 line 16
Claims 20-21:	Previous claim 8; page 16 lines 17-26; Example 7 (page 43 ff.)
Claims 22-23:	Previous claim 8; Example 9 (page 45 ff.); Example 11 (page 47 ff.)
Claims 24-25:	Previous claim 6; Example 9 (page 45 ff.); Example 11 (page 47 ff.)
Claims 26-28:	As for claim 13

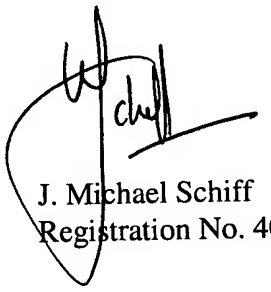
Applicants respectfully request examination of the application on the merits in view of these amendments.

Conclusion

The new claim set consists of 16 claims, of which 3 are independent. Accordingly, no fee is believed payable with respect to this Amendment.

Nevertheless, should the Patent Office determine that any fee is required for further consideration of the application, the Assistant Commissioner is hereby authorized to charge such fee (or credit any overpayment) to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,



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February 20, 2002

Version with Markings to show

CHANGES MADE

USSN 10/001,267
Docket 093/004p

Amended Title:

~~HEPATOCYTE LINEAGE CELLS~~
~~DERIVED FROM PLURIPOTENT STEM CELLS~~

PROCESS FOR MAKING HEPATOCYTES
FROM PLURIPOTENT STEM CELLS

Amendment to Specification:

[page 2, lines 13-18]

This application is a continuation-in-part of ~~USSN 09/718,308, filed November 20, 2001;~~ USSN 09/872,182, filed May 31, 2001; and International Patent Application PCT/US01/13471, filed April 26, 2001, ~~designating the U.S., to be published in English 18 months after the first priority date pursuant to Article 21(2) of the PCT~~ which designates the U.S. and was published as WO 01/81549 on November 1, 2001. This application also claims priority to U.S. provisional patent application 60/200,095, filed April 27, 2000. The ~~four~~ three priority applications and U.S. utility application 09/718,308 are hereby incorporated herein by reference in their entirety.

New claims:

13. *(New)* A method for producing differentiated cells from primate pluripotent stem (pPS) cells, comprising culturing the pPS cells or their progeny in a medium containing a histone deacetylase inhibitor, until at least ~60% of the cultured cells have at least three of the following characteristics:
    - antibody-detectable expression of α_1-antitrypsin (AAT);
    - antibody-detectable expression of albumin;
    - absence of antibody-detectable expression of α-fetoprotein;
    - RT-PCR detectable expression of asialoglycoprotein receptor (ASGR);
    - evidence of glycogen storage;
    - evidence of cytochrome p450 activity;
    - evidence of glucose-6-phosphatase activity; or
    - the morphological features of hepatocytes.

14. *(New)* The method of claim 13, wherein at least about 60% of the cells have at least five of said characteristics.

15. *(New)* The method of claim 13, wherein at least about 80% of the cells have at least seven of said characteristics.

16. *(New)* The method of claim 13, wherein the histone deacetylase inhibitor is n-butyrate.

17. *(New)* The method of claim 13, wherein the histone deacetylase inhibitor is propionic acid, isovaleric acid, or isobutyric acid.

18. *(New)* The method of claim 13, wherein the histone deacetylase inhibitor is Trichostatin A

19. *(New)* The method of claim 13, comprising pre-differentiating the cells by forming embryoid bodies.

20. *(New)* The method of claim 13, comprising pre-differentiating the cells by culturing in a medium containing dimethyl sulfoxide (DMSO), dimethylacetamide (DMA), hexmethylene bisacetamide, or another polymethylene bisacetamide.

21. *(New)* The method of claim 13, comprising further culturing the cells in a medium containing a cytokine or hormone selected from glucocorticoids, epidermal growth factor (EGF), insulin, TGF-α,

TGF-β, fibroblast growth factor (FGF), hepatocyte growth factor (HGF), IL-1, IL-6, IGF-I, IGF-II, and HBGF-1.

22. *(New)* The method of claim 21, wherein the cells are cultured in a medium containing at least three of said cytokines or hormones.

23. *(New)* The method of claim 22, wherein the cells are cultured in a medium containing EGF, TGF-α, and HGF.

24. *(New)* The method of claim 13, further comprising maintaining the differentiated cells by culturing them in a medium containing a histone deacetylase inhibitor.

25. *(New)* The method of claim 13, further comprising maintaining the differentiated cells by culturing them in a medium containing n-butyrate.

26. *(New)* The method of claim 13, wherein the pPS cells are human embryonic stem (hES) cells.

27. *(New)* A method for maintaining cells differentiated from primate pluripotent stem (pPS) cells, comprising culturing the differentiated cells in a medium containing a histone deacetylase inhibitor, so that at least ~60% of the cultured cells maintain at least three of the following characteristics:
    - antibody-detectable expression of α_1-antitrypsin (AAT);
    - antibody-detectable expression of albumin;
    - absence of antibody-detectable expression of α-fetoprotein;
    - RT-PCR detectable expression of asialoglycoprotein receptor (ASGR);
    - evidence of glycogen storage;
    - evidence of cytochrome p450 activity;
    - evidence of glucose-6-phosphatase activity; or
    - the morphological features of hepatocytes.

28. *(New)* A method for producing differentiated cells from human embryonic stem (hES) cells, comprising culturing the hES cells or their progeny in a medium containing a histone deacetylase inhibitor, until at least ~60% of the cultured cells have at least three of the following characteristics:

- antibody-detectable expression of α_1-antitrypsin (AAT);
- antibody-detectable expression of albumin;
- absence of antibody-detectable expression of α-fetoprotein;
- RT-PCR detectable expression of asialoglycoprotein receptor (ASGR);
- evidence of glycogen storage;
- evidence of cytochrome p450 activity;
- evidence of glucose-6-phosphatase activity; or
- the morphological features of hepatocytes.